



Research Spotlight

Brown University Receives Clinical and Translational Science Award Planning Grant

Timothy P. Flanigan, MD

The NIH has initiated a new program entitled “Clinical and Translational Science Awards” (CTSA) to transform clinical research by accelerating discoveries in order to improve patient care. The objectives of the CTSA are: 1) to develop a distinct discipline for clinical and translational science at institutions across the country; 2) to provide opportunities and resources for original research on novel methods; 3) to utilize novel technologies for the full spectrum of clinical and translational science; 4) to synergize partnerships with industry foundations and community physicians and; 5) to train the interdisciplinary teams who will conduct the clinical and translational research of the future.

The NIH believes that the CTSA process will create, among universities and health science centers, an integrated environment for clinical and translational research. This will provide an academic home, support for protocol preparation, regulatory compliance and data management, education leading to advanced degrees in clinical research and specialized cores and services to support translational research.

The NIH envisions that the CTSA programs will replace the current General Clinical Research Centers (GCRCs) around the country. Brown University in collaboration with Rhode Island Hospital, The Miriam Hospital, Memorial Hospital of Rhode Island, Women and Infants Hospital and the University of Rhode Island, has been awarded a one-year planning grant in the amount of \$150,000. Dr. Timothy P. Flanigan is Principal Investigator of this grant and Dr. Alan Rosmarin will serve as Co-PI. This grant will provide resources to help with the development of a full CTSA application within in the next two years. The funding for the full grant, which incorporates advanced clinical education in clinical and translation research as well as the development of specialized cores and multi-disciplinary scientific “think tanks”, is \$4 million per year.

The NIH has defined translational research in two areas; 1) the process of applying discoveries generated during laboratory research in the pre-clinical phase of development of trials with human participants and 2) research aimed at enhancing the adoption of best practices in the community. The planning grant awarded to Brown University envisions the state of Rhode Island in collaboration with the Department of Health, universities and health science centers as an ideal model to evaluate the adoption of best

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Dr. Alan Rosmarin, Ms. Jennifer Hyde and Dr. Timothy Flanigan

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Chairman's Message

Edward J. Wing, MD



Dean Eli Adashi and Provost David Kertzer have launched one of the most exciting initiatives at the Brown Medical School in recent years. A Strategic Plan Working Group has been established to make recommendations to the Brown Corporation regarding 1) the restructuring and improvement of relations between Brown and the Lifespan

Hospitals and 2) the relocation of the medical school. The Working Group includes Tim Flanigan, Sue Cu-Uvin, and myself from the Department of Medicine. I believe that this effort is vital to the future growth and success of the entire school. In many ways, we have reached the limits of our growth in our current fractionated system. The new structure will hopefully allow the school and the hospitals to develop a single strategic planning and implementation process. Resources from both institutions will be used to grow innovative programs that will take all of us to the next level excellence. For example, the development of an academic comprehensive cancer center will benefit the institutions, the faculty, and most importantly our patients. A timely example of the commitment of Brown to investment in the medical school is the agreement, made October 24, to purchase seven buildings in the Jewelry District. This commitment will invigorate scientific growth in this area even further. An example of a recent joint planning process resulting in a success is the CTSA planning grant described in this newsletter. Furthermore, the relocation of the medical school to the RIH campus will align the clinical mission with our educational and research mission.

As usual, the continuing success of the Department as illustrated by successful programs and individuals is described in the newsletter. It is also a great pleasure to congratulate the recently selected chief residents for the academic year 2007–8.

practices within the community and the impact it can have on the health of all Rhode Islanders. Brown's history of working with vulnerable populations including minority communities, incarcerated persons, substance users, and the poor and disenfranchised makes it ideally suited to implement and evaluate community-wide interventions.

The Brown Planning Grant propose three components: 1) "Collaboratories" which will bring together laboratory and clinical scientists in an intellectual home to develop clinical and translational science; 2) a series of cores which will provide services related to pilot projects and new grant proposals for junior and senior investigators in the area of clinical and translational science; 3) a dedicated curriculum addressing clinical and translational science for graduate and medical students, fellows, and junior faculty which could lead to a Masters Degree in Clinical and Translational Science and, in future, a PhD in the same discipline.

Collaboratories will be defined by their transformative vision and energy. It will be cross-disciplinary and cross-departmental and not focus on one disease or one discipline. The collaboratory can be thought of as a scientific generator. Proposed collaboratories include:

1. Emerging Technologies
2. Novel Therapeutics
3. Population and Community Based Interventions
4. Global Health
5. Gene Environment Interactions

Proposed cores include:

1. Genomics/Proteomics
2. Molecular Pathology
3. Statistics/Bioinformatics
4. Clinical Trials Unit
5. Regulatory/IRB
6. Ethics
7. Pharmacokinetics and Drug Delivery
8. Minority and Women Investigators
9. Community Participation
10. Biotechnology/Intellectual Property/Patents/Industry
11. Imaging

A proposed integral component of the clinical and translational science award is education, training and career development in clinical and translational sciences. This educational component should integrate closely with K award and T award grants throughout the university and partnering hospitals.

Although the grantee institution is Brown University, the planning grant is a collaborative project including the strengths of URI (especially the Schools of Nursing, Pharmacy and Life Sciences) and all the Brown affiliated hospitals.

Interested individuals should contact the PI of the planning grant, Dr. Timothy Flanigan (TFlanigan@Lifespan.org), Co-PI Dr. Alan Rosmarin (Alan_Rosmarin@Brown.edu) or the administrative coordinator Jennifer Hyde (Jhyde@Lifespan.org).

Interventional Pulmonology at Rhode Island Hospital

Muhanned Abu-Hijleh, MD FCCP

As the number and complexity of endoscopic pulmonary procedures increased over the last three decades, Interventional Pulmonology gradually developed as one of the sub-specialties in Pulmonary and Critical Care Medicine. In 2002, the American Thoracic Society, in a joint statement with the European Respiratory Society published the first guidelines that dealt with this subspecialty. This was followed by guidelines from the American College of Chest Physicians in 2003.

Interventional Pulmonology deals with various endoscopic airways and pleural procedures and techniques. This includes using bronchoscopy and medical thoracoscopy (pleuroscopy) in diagnostic and therapeutic interventions for various malignant and benign disorders. The use of fluoroscopic and ultrasound guidance during such procedures is required during some procedures.

Diagnostic flexible bronchoscopy includes bronchial washing, bronchoalveolar lavage, transbronchial needle aspiration, endobronchial needle aspiration, transbronchial biopsies, endobronchial biopsies, and cytology/ microbiology brush samples. This is done with or without fluoroscopy guidance depending on the specific patient condition. The endobronchial ultrasound was recently introduced to visualize the airway wall (not only the inner surface) and lymph nodes or other structures adjacent to the airways, using ultrasound waves. This helps to localize biopsy targets around to the central airways, and can assess the airway wall involvement by different conditions.

Therapeutic flexible or rigid bronchoscopy (or a combination of both) is performed to extract foreign bodies, and for re-canalization of the airways that are occluded by different malignant and benign conditions. This includes using Laser therapy, Electrocautery and Argon Plasma Coagulation, Cryotherapy, Photodynamic Therapy and other advanced procedures.

Localized delivery of radiation therapy (Brachytherapy) for airways' involvement with malignancy is done in conjunction with our colleagues in Radiation Oncology. Airway stenting is done using different stent types to re-establish the patency of central airways that are compressed by primary or metastatic lung malignancies. This is rarely used for benign disease.

Diagnostic bronchoscopies are done for a wide range of benign inflammatory and infectious conditions. Diagnosing and staging lung malignancies is the other major indication for diagnostic bronchoscopy. The majority of therapeutic bronchoscopy procedures are done for palliation of dyspnea or other symptoms that develop in patients with advanced primary or metastatic lung malignancy.

Pleural procedures include thoracentesis, closed pleural biopsies and medical thoracoscopy (pleuroscopy). Such procedures are done to evaluate a variety of benign and malignant conditions associated with pleural effusions. Placement of chest tubes (including chronic indwelling tubes tunneled under the skin) and performing chemical pleurodesis are common procedures. Such procedures are essential in the management of malignant pleural effusions.

Interventional Pulmonologists at Rhode Island Hospital work closely with colleagues in Thoracic Surgery, General Surgery, Medical Oncology, Radiation Oncology and Radiology departments. Our goal is to provide the best possible services to our patients as members of a multidisciplinary approach team, in the safest and most efficient manner. The available Interventional Pulmonology services and nature of procedures in our institution developed over the last three years. The continuous support from the department of medicine and our institution was essential to this progress. We provide most of the abovementioned diagnostic and therapeutic procedures with few exceptions.



Our staff includes two Pulmonologists with Interventional interest and training, well qualified pulmonary function test technicians that assist during bronchoscopies, an Interventional Pulmonology nurse coordinator, and two sedation nurses in the special procedures unit. Our fellows are involved in the bronchoscopy suite as part of their training.

As we are part of the department of medicine, we continue to have the commitment to train and supervise medical residents in various procedures. This includes primarily thoracentesis. Other procedures include training residents in vascular access and other medical procedures in the intensive care unit. Our goal is to ensure adequate exposure and competence of residents in such procedures.

Research is an integral part of our division. The Pulmonary, Critical Care and Sleep division was recently awarded an industry grant to be part of randomized multi-center trial that involves bronchoscopic volume reduction for emphysema. This involves using endobronchial one-way valve devices that are implanted in the airways to improve ventilation in emphysema patients. We are in the process of applying to our IRB and going through the appropriate channels prior to starting screening and enrollment.

Our future goals include expanding this service as the need increase. We will continue

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Transplant-related LCMV Outbreak Identified at Rhode Island Hospital

Staci Fisher, MD

In April 2005, two men were admitted to Rhode Island Hospital with fever and diarrhea. They had each undergone renal transplantation three weeks before. On physical exam, both had erythema overlying the allograft kidney. Their creatinines were stable but their transaminases elevated, and routine cultures of stool, urine and blood were negative. Ultrasound and CT scans of the abdomen and pelvis were unremarkable.

They lived in different cities in Rhode Island, but attended the same dialysis center. Neither had family members who were ill. They shared a common organ donor, who had died of a cerebrovascular accident complicating hypertension; she had no fever or other signs to suggest infection. An autopsy had been performed following organ procurement that revealed a hemorrhagic stroke, with no evidence of infection.

The possibility of donor-transmitted infection was raised after Dr. Staci Fischer discovered that each of the recipients of organs from the donor were ill; two patients in Boston and the two at Rhode Island Hospital. An investigation involving the New England Organ Bank, the Rhode Island Department of Health, the Massachusetts Department of Health and the Centers for Disease Control and Prevention (CDC) ensued. All four patients had fever and diarrhea. Pulmonary infiltrates, renal failure, headache and seizures were variably present. In discussions with the transplant and infectious disease physicians caring for the lung and liver recipients, extensive testing including tissue biopsies and cultures had been performed, with no etiology identified in each case.

Within 5 days of beginning the investigation, three of the four recipients had died. Tissues and blood from each of the recipients and the organ donor were sent to the CDC for additional testing. There, investigators performed immunohistochemical staining on tissues to look for a number of pathogens known to be transmitted via organ transplantation, including adenovirus, rabies and West Nile virus. Testing for lymphocytic choriomeningitis virus (LCMV) was positive in tissues from each of the organ recipients. While never published, a previous outbreak of infection with this virus had occurred in Wisconsin and Minnesota in 2003 in which all four organ transplant recipients died. Extensive testing of donor tissues in both outbreaks revealed no evidence of infection with LCMV.

The surviving patient, one of the Rhode Island Hospital kidney recipients, had his immunosuppression decreased and was started on ribavirin, based on data supporting its use in the treatment of a related virus, Lassa fever, seen predominantly in Africa. He recovered well and enjoys excellent allograft function.

LCMV, a virus which causes asymptomatic infection or aseptic meningitis in the majority of patients, may cause lifelong, asymptomatic infection in house mice. Outbreaks have been associated with infection of pet hamsters and laboratory rodents.

A pet hamster, purchased three weeks prior to the onset of the donor's stroke, was found in her home. While the donor had minimal contact with the animal, her daughter, who was well, was found to have IgG and IgM antibodies to LCMV. The hamster was sacrificed and found to have PCR, culture and histopathologic evidence of LCMV infection in every tissue tested by the CDC. The hamster LCMV strain was found to be identical to that isolated from all four organ recipients.

A large public health investigation was initiated. The remaining hamsters and guinea pigs in the pet store from which the hamster was purchased were euthanized. Three were found to be infected with an LCMV strain with < 0.5% genetic divergence from the cluster strain. The animals were traced to a distributor in Ohio, which was found to have violations in biosafety procedures, including mixing of wild mice with the pet hamsters and guinea pigs obtained from breeders. The Arkansas breeder who most likely supplied the hamsters to the distributor was to be investigated, but destroyed the remaining hamsters (some 10,000 or more, reportedly) before public health officials arrived.

The investigation was published in the *New England Journal of Medicine* on May 25, 2006, along with the 2003 Midwestern outbreak. Efforts are underway on a national level – involving the CDC and the United Network for Organ Sharing – to create a tracking system for infections complicating solid organ transplantation, so that outbreaks of infection may be identified earlier and public health investigations expedited in the hope of improving clinical outcomes.

Staci Fisher, MD, is an Assistant Professor and Director, Transplant Infectious Diseases, Rhode Island Hospital.



Department of Medicine Vascular Research Laboratory (VRL)–VAMC

Sharon Rounds, MD

The Vascular Research Laboratory (VRL) of the Department of Medicine at Brown Medical School is located at the Providence VA Medical Center in Building 35. The Vascular Research Laboratory is an interdisciplinary group of scientists and clinicians with the overall goal of translating basic insights in vascular function into clinical practice. Current research ranges in scope from cell biology using cultured cells to animal studies to health services research. The philosophy guiding VRL research is that better treatments for vascular diseases are based on thorough understanding of normal and abnormal vascular cell function. Originally the group was focused on the lung circulation, but research interests have expanded to include heart function and systemic vascular function. Research collaborators are diverse, from the departments of Medicine, Surgery, Molecular Pharmacology Physiology and Biotechnology, Pathology, and Community Health.

The Principal Investigators are from Pulmonary/Critical Care (Elizabeth Harrington, PhD, Associate Professor; James Klinger, MD, Associate Professor; Qing Lu, PhD, Assistant Professor; Sharon Rounds, MD, Professor) and Cardiology (Gaurav Choudhary, MD, Assistant Professor; Wen-Chih (“Hank”) Wu, Assistant Professor) in the Department of Medicine at the VA and RIH. Affiliated faculty includes Linda Nici, MD, Clinical Associate Professor, Pulmonary/Critical Care, and Paul Pirraglia, MD, Assistant Professor, General Internal Medicine. Current trainees in the VRL include Matt Jankowich, Pulmonary/Critical Care fellow, and Akua Owusu-Sarfo, Brown Pathobiology graduate student. This summer has brought the usual influx of undergraduate research students, including Cicely Grate from Claflin University, Alper Celik, Angela Wang, Aaron Simon, and Reshma

Ramachandran from Brown University. The group is supported by skilled research assistants,

led by Julie Newton. Cardiology fellows, Shalin Mehta, Victor Shin and Marayam Afshar, are pursuing translational studies involving flow mediated vasodilation and cardiac CT.

Faculty research interests are diverse, but focus on mechanisms of vascular injury and mechanisms of maintenance of normal vascular function. Research funding sources are similarly diverse and include both peer-reviewed external funding as well as corporate support. Gaurav Choudhary is funded by the Rhode Island Foundation to study the role of C-type Natriuretic Peptide in hypoxia. Beth Harrington is funded by NIH RO1 and VA Merit Review grants for study of endothelial barrier function modulation by PKCdelta and study of signaling in hypoxic pulmonary vs. systemic endothelium. Jim Klinger has funding from an American Heart Association Established Investigator Award for study of atrial natriuretic peptides in right ventricular hypertrophy. Qing Lu has a prestigious Parker B. Francis Foundation Fellowship and a research grant from the American Lung Association to support her studies of TGFbeta effects on endothelial barrier function. Sharon Rounds studies the effects of small GTPase methylation on endothelial cell apoptosis and barrier function with funding from NIH RO1 and VA Merit Review grants. Hank Wu has VA Merit Review and TREP grants to study surgical transfusion practices and cardiovascular outcomes. In addition, Jim Klinger has an active research program in treatment of pulmonary hypertension and Gaurav Choudhary and Hank Wu are conducting clinical studies of cardiac and vascular function.

Since 1998, the VRL has occupied 2500 square feet of space, plus 3 associated offices in the new Research Building at the PVAMC. The space consists of very well equipped shared general lab space plus shared facilities for imaging, tissue culture, and heavy equipment. In 2005-06 Elizabeth Harrington



successfully applied for a \$150,000 equipment grant from the VA that has allowed the group to obtain a sophisticated Nikon live cell imaging system and a specialized hypoxia chamber.

Total direct costs on non-corporate, peer-reviewed grants awarded to VRL investigators in 2001–06 were \$4.5 million. The 2005–06 academic year has been marked by funding of NIH RO1’s to Sharon Rounds and Beth Harrington with annual direct costs of \$200,000 and \$250,000, respectively. The group was very pleased recently to learn that Akua Owusu-Sarfo has been awarded a pre-doctoral training fellowship from the American Heart Association for \$21,000 per year for two years to support her graduate studies, mentored by Beth Harrington.

The Vascular Research Laboratory investigators have been productive in terms of scholarly activity with 34 publications in 2004-06. There have been 19 research trainees doing mentored research in the VRL in 2004-06. The PI’s have also contributed to the profession with 4 journal editorial board positions and 9 study section memberships in 2004-06.

The Vascular Research Laboratory investigators have active research collaborations with colleagues at Brown and elsewhere. We encourage trainees interested in pulmonary/critical care, cardiology, and vascular diseases to visit the lab and consider engaging in vascular research. We also welcome visitors to the laboratory at the Providence VA Medical Center and to our website at www.brown.edu/Research/Vascular_Research_Laboratory. Check it out!

Research Awards

Edward Filardo, PhD, in the Division of Medical Oncology has received a one year Concept Award from the Department of Defense for a project titled 'Assessment of GPR30, A Seven-Transmembrane Estrogen Receptor, as an Oncogene.' The \$75,000 in direct cost funding will be used to investigate whether hyperexpression of wild-type or constitutively active GPR30, a seven transmembrane-spanning receptor, in mammary duct epithelia of transgenic mice is associated with a predisposition for the development of breast carcinoma.

Stephen Moss, MD, in the Division of Gastroenterology, received a 5-year R01 grant from the National Cancer Institute at NIH for a project titled 'p27 and Apoptosis Resistance in Gastric Cancer. Funding approximates \$135,000 per year in direct costs. This grant has three specific aims: 1) Determine how *H. Pylori* increases the proteasomal degradation of p27 protein. 2) Characterize the histological, bacterial, and immunological aspects of our novel model of *H. Pylori*-associated gastric cancer in p27-deficient mice. 3) Utilize the p27-deficient mouse as a preclinical tool to test the effects of *H pylori* eradication on gastric cancer susceptibility.

Michael Stein, MD, in the General Internal Medicine Division, has received a 5-year K-24 Midcareer Investigator Award in Patient Oriented Research from the National Institute of Drug Abuse. The approximately \$110k per year in direct costs will allow Dr. Stein to develop, implement, and evaluate the efficacy and effectiveness of behavioral interventions for complex drug abusing patients in new treatment settings. Specifically, the aims are to 1) provide scientific and administrative leadership for the young investigators based in the Substance Abuse Research Unit. 2) provide training support for drug abuse treatment and services research, including support for junior faculty.

Michael Stein, MD, in the General Internal Medicine Division, has received a R01 from the National Institute on Drug Abuse for a project titled 'Antidepressants During Office-based Buprenorphine.' Three years of funding at over \$250k per year in direct costs will be used towards the following specific aims: 1) To perform a randomized, double blind, placebo-controlled trial to determine whether escitalopram treatment of depressive symptoms increases treatment retention among opioid dependent 182 patients initiating office-based buprenorphine treatment. 2) To determine if antidepressant medication treatment reduces depressive symptom scores compared to a placebo condition among office-based buprenorphine treatment recipients.

Research News

Laboratory of Retrovirology Awarded NIH Cooperative Grant for Microbicide Work

Bharat Ramratnam, MD

Bharat Ramratnam, MD, Division of Infectious Diseases has been awarded a U-19 multi-project cooperative grant from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, to develop a new generation of therapies aimed at HIV-1, Herpes Simplex Virus (HSV) and Human Papilloma Virus (HPV). The U19 cooperative agreement involves numerous institutions including Rhode Island Hospital, Mt. Sinai Medical Center (NY), University of Wisconsin, New England Primate Research Center of Harvard University, Duke University, University of New Mexico, Tulane Primate Center, Southwest Research Institute and the University of Chicago. RIH will serve as the lead institution.

The investigators will create new drugs based upon the biology of RNA interference (RNAi). RNAi refers to post-transcriptional and post-translational gene silencing by short interfering RNA (siRNA). Using a variety of animal models, the investigators will determine whether siRNA targeting host and viral proteins prevents HIV-1, HSV and HPV transmission and replication *in vitro* and *in vivo* using relevant animal models. As proof-of-principle studies are completed, the investigators will formulate their siRNA preparations for direct application to mucosal surfaces. Besides antiviral efficacy, the project will rigorously address the toxicology profile of siRNA drugs and thereby serve as a foundation for planning future phase I studies in normal human volunteers.



Division of Cardiology Update

Alfred Buxton, MD

The Cardiology Division Faculty continues to grow in numbers and services offered. Peripheral vascular disease, often undiagnosed and under treated, is being recognized with increasing frequency as a significant cause of cardiovascular morbidity. At The Miriam Hospital, **Imdad Sadiq, M.D.**, joined the Division one year ago after completing a Peripheral Vascular Interventional and Non-invasive Vascular Medicine Fellowship at Saint Elizabeth's Hospital, Boston, and an Interventional Cardiology Fellowship at Hartford Hospital. Dr. Sadiq has established a non-invasive peripheral vascular diagnostic laboratory and an active peripheral interventional service. A similar expansion of noninvasive diagnostic inpatient and outpatient services for peripheral vascular disease is taking place at Rhode Island Hospital, and plans are underway for collaborative investigations involving both Rhode Island and Miriam Hospitals. These cooperative studies will draw on the strengths and patient populations of both Hospitals.

The nuclear cardiology section at RIH continues to grow under the direction of **James A. Arrighi, MD**. During the past year, cardiac PET has been established clinically at Brown. At present, the lab provides FDG cardiac viability studies. Over the winter, rest/stress myocardial perfusion PET will be established. A number of research programs are in progress in the section of nuclear cardiology. Two protocols involve the assessment of sympathetic cardiac innervation in patients with heart failure and arrhythmias, using a novel imaging agent called MIBG, that is taken up by sympathetic nerve endings. These studies will help determine whether MIBG imaging provides additional prognostic information in these patients. Another project, using PET imaging, examines the feasibility of assessing radio labeled glucose uptake in carotid atherosclerotic plaques as a means to determine plaque instability. The lab also is participating in a registry of "high tech"

modalities (SPECT, CT, and PET). Finally, the Nuclear Cardiology Database Program continues to serve as a resource for residents and fellows to perform research. Dr. Arrighi has been appointed Vice President of the Certification Board for Nuclear Cardiology. In addition, **Brian Abbott, MD** of the faculty, has been appointed Program Chair for the next annual meeting and scientific sessions of the American Society of Nuclear Cardiology.

The Cardiovascular Research Center (CVRC), the basic science arm of the Division is poised to move into new laboratory facilities in the Coro Building after the first of the year. **Gideon Koren, M.D.**, the Director, whose research has been focused on function and abnormalities of cardiac potassium channels, has developed a unique rabbit model of the long QT syndrome. The rabbits experience spontaneous cardiac arrests similar to those observed in humans. This work led to Dr. Koren heading a multi-center international consortium that has just submitted a cluster grant application to the NHLBI to study the contribution of ion channel defects to sudden cardiac death in humans. **Ulrike Mende, M.D.**, Associate Professor of Medicine in the CVRC is actively investigating the role of G proteins in the regulation of myocyte hypertrophy and failure.

Athena Poppas, M.D., Director of the Echocardiography laboratory at RIH has been Chair of the American College of Cardiology's Women in Cardiology Committee. She is leading this committee on a varied agenda, which includes a Visiting Professor Program, which seeks to provide mentoring and an opportunity for interaction with female medical students and residents considering a career in cardiology. Dr. Poppas is also serving as section editor for the American College of Cardiology's Echocardiography Self-Assessment module. Dr. Poppas has become recognized as an expert in heart disease during pregnancy. In recognition of her expertise, she delivered Cardiology Grand Rounds on this topic at Massachusetts General Hospital earlier this year.



On Monday October 23, 2006, **Drs. David O. Williams** and **J. Dawn Abbott** presented the one-year results of the DEScover Registry as part of the Late Breaking Clinical Trial session at the Transcatheter Therapeutics (TCT) meeting in Washington DC. This meeting is the largest scientific and educational program dedicated to cardiac catheter intervention the world with more than 7,000 attendees.

DEScover is a prospective observational investigation designed to determine the types and outcomes of catheter-based coronary interventions performed in the United States. Dr. Williams serves as the national Principal Investigator. A total of 7,752 consecutive patients treated by PCI were enrolled at 140 clinical centers during 2005. A unique electronic distributed data entry system was utilized to capture baseline clinical and procedural characteristics as well as in-hospital events. Following discharge, patients were evaluated at 6-weeks, 6-months and at one-year by trained data coordinators. At least one-stent was implanted in 96% of patients and of these 94% received a drug-eluting stent (DES). Patients treated with a bare metal stent (BMS) experienced higher rates of death and repeat revascularization at one-year. Following adjustment for baseline differences, DES patients still were less likely to require either CABG or repeat PCI during follow-up. Importantly this benefit was achieved without excess death, MI or stent thrombosis among DES patients. In addition, patients treated with a sirolimus DES were compared to those receiving a paclitaxel DES.

No differences in repeat revascularization or other adverse events were observed between these two groups. Concomitant with the presentation in Washington, the DEScover manuscript was published by *Circulation*.

Profiles

Facing the Challenge of Caring for HIV-Infected Women

Susan Cu-Uvin, MD came to Brown Medical School in 1992 to join the Departments of Medicine and Obstetrics and Gynecology to focus on the tremendous challenges facing women with HIV worldwide. Since coming here in 1992, she has spearheaded a highly successful program that has described the dynamics of HIV within the genital tract of women, which has implications for both vertical transmission from mother to child and heterosexual transmission. Her work which has been continually funded through a NIH RO1 for the last nine years has characterized HIV shedding within in the genital tract and the response to highly active antiretroviral therapy. This work has demonstrated that suppression within the blood usually results in suppression within the genital tract. However, intermittent genital tract shedding of HIV occurs even in women with good viral suppression in the blood and that resistance patterns in the blood may vary from the genital tract. Her recent work has focused on the impact of bacterial vaginosis and herpes simplex virus in the genital tract and the potential to up-regulate HIV. Her team is also assessing antiretroviral drug levels in the genital tract.

Susan has served on the special IOM Committee evaluating methods to better prevent mother to child transmission of HIV in the United States. She has served as the chair for the Women's Health Committee of the Adult AIDS Clinical Trials Group as well as working to develop "cross-program" protocols to prevent vertical transmission and to improve treatment for HIV infection among women worldwide. She has been involved with the HIV prevention and vaccine trials as well as work in microbicides.

Susan has developed a special program addressing the challenges of HIV among menopausal women. As women with HIV age and are able to prevent the complications of HIV/AIDS through HAART, they are facing long term issues such as osteoporosis, diabetes, cardiac, hepatic and renal disease. This work is being funded through the CDC SUN Study.



Photo Courtesy of Ladies Home Journal

Dr. Susan Cu-Uvin

A key focus of this study is to characterize HPV infection and prevent its long term consequences.

Susan has served as mentor for countless medical students, residents, fellows and other junior faculty. She has been able to bridge the gap between Ob/Gyn and Medicine very successfully which has been of tremendous benefit to women with HIV infection both here in Rhode Island and globally.

Recently, Dr. Cu-Uvin was the recipient of the inaugural Health Breakthrough Award from the Ladies Home Journal for establishing the first HIV and menopause clinic in the world. The award recognizes medical leaders in making life-saving and life-enhancing discoveries in treatment, research and diagnostics.

Geriatrics for the Practicing Physician

Ana Tuya, MD

The Division of Geriatrics is pleased to announce the start of a regular column on geriatrics in *Medicine & Health Rhode Island*. The column will be titled *Geriatrics for the Practicing Physician*, and will focus on practical approaches to geriatrics topics and issues to aid primary care physicians and specialists in caring for the growing older patient population in our State. Topics will include useful tools for assessing health and function in older adults; managing common

problems, such as falls, insomnia, and cognitive impairment; and useful resources for education and community referral sources. Contributions will be made by faculty within the Division and by geriatricians practicing in the community. Please contact Ana Tuya, MD, Editor, for the column at atuya@lifespan.org, with suggestions for topics that you would like to see addressed in the column.

Visit our website at: www.brownmedicine.org

Division of Nephrology Academic Update

Lance Dworkin, MD

Moses Aboagye-Kumi, MD, Renal Fellow, was awarded the Haffnerreffer Award, 2006

Dr. Aboagye-Kumi and Susan Eckert, MD, medical resident, winners of the American College of Physicians 2006 Associate's Forum Competition held on May 10, 2006 at the Radisson Airport Hotel, Warwick, RI. Their research was conducted in the Renal Division under the direction of Lance Dworkin, MD and Rujun Gong, MD, PhD.

Lance Dworkin, MD, Professor of Medicine, Vice Chairman of Medicine. Director, Division of Renal Diseases. Gave the following lectures: Emory University, Renal Grand Rounds. On Beyond ACE's: Uncovering the Multiple Renal Protective Actions of HGF. Atlanta, GA, March 28, 2006.

Holy Name Hospital/Medical Society of New Jersey. Renal Vascular Disease: Diagnosis, Treatment, and Clinical Study Symposium. "Controversial Treatments of RAS". Newark, NJ. April 5, 2006.

American Society of Hypertension 21st Annual Scientific Meeting and Exposition: Characterizing the Hypertension Phenotypes "The Controversial Treatment of Renal Artery Stenosis: The CORAL Trial". New York, NY. May 19, 2006.

Reginald Gohh, MD. Associate Professor of Medicine. Medical Director, Division of Transplantation.

Medicine Grand Rounds, Roger Williams Hospital, April 2006 "Focal Segmental Glomerulosclerosis and its Post-Transplant Recurrence"

Douglas Shemin, MD, Associate Professor of Medicine. Associate Director for Clinical Affairs, Division of Renal Diseases was named "Outstanding Medical Professional of the Year" by the National Kidney Foundation of Massachusetts, Rhode Island, New Hampshire, and Vermont for 2005.



2008–2009 Chief Medical Residents Announcement

We are very pleased to announce that Drs. Kathleen Doyle, Ravi Gupta, Anthony Lizzaraga, Edmund Sears and Sarah Tapyrik have accepted a position as Chief Medical Resident, Brown Internal Medicine Residency Programs for the academic year of 2008–2009. Please join us in congratulating these outstanding individuals!

Internal Medicine Residency Programs
Department of Medicine
Rhode Island Hospital and The Miriam Hospital
and the VAMC
Brown Medical School
Providence, RI

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Interventional Pulmonology at Rhode Island Hospital

to work closely with all of our colleagues in the institution and the community. Acquiring the necessary technology and equipment to complement the current services will be essential to provide the best possible services. This includes continuous education and training of team members. Regional and national recognition will be the next challenge over the following five years.

*The Department of
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is published quarterly.*



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Division of Rheumatology Update

Edward Lally, MD



Dr. Edward Lally joined the Brown Medical School, Department of Medicine at Rhode Island Hospital as Director of the Division of Rheumatology in March 2005. Here he has outlined the division's goals and objectives for the near future. The clinical and administrative offices for the Division of Rheumatology are located at 2 Dudley Street in the Medical Office Center, Suite 370.

The division will pursue a program of growth and development that involves four major areas: patient care, basic research, clinical research and education. In the area of patient care, Dr. Lally intends to continue the delivery of high quality rheumatologic services that have been provided by Dr. Stuart Schwartz since 1989. Ambulatory rheumatologic care is available in the Division offices at the Medical Office Center, 2 Dudley Street, as well as in the Rheumatology Clinic at Rhode Island Hospital. The Division also offers an Inpatient Rheumatology Consultation Service. Dr. Lally foresees expansion of the existing comprehensive rheumatologic care for both outpatients and inpatients through the recruitment of additional clinical rheumatologists.

Dr. Lally is also committed to a developing basic science research program within the Division of Rheumatology. He is currently in the process of recruiting basic investigators in two major areas. The first is the area of bone and cartilage biology. These individuals will have expertise in biologic processes involving bone, cartilage and synovium. These include inflammation, cytokine networks and cell signaling. There is close collaboration planned with the Department of Orthopedic Surgery in this regard. The other major basic science research area is in autoimmunity. Basic investigators interested in the autoimmune diseases, particularly focused on systemic lupus erythematosus and scleroderma will be sought after.

Clinical research is of paramount importance within the Division of Rheumatology. Individuals who have an interest in osteoarthritis as well as in autoimmune diseases will be recruited. It is anticipated that those with expertise in epidemiology and outcomes research will be a strong part of the research effort in the Division of Rheumatology. It is anticipated that affiliations with the planned School of Public Health at Brown will be an attraction for such investigators. Currently the Division of Rheumatology participates in the Osteoarthritis Initiative, an NIH-sponsored cohort analysis of people at risk for osteoarthritis. Dr. Lally serves as the Brown Medical School Site Director for the Scleroderma Clinical Trials Consortium, an international group of rheumatologists involved in therapeutic trials for scleroderma and related diseases.

Educational goals of the Division are also a high priority. Dr. Lally is in the process of applying to the ACGME for a Brown Medical School Rheumatology Fellowship Training Program. It is expected that two Rheumatology Fellows (1 per year) will train at Rhode Island Hospital and at its affiliated hospitals within the next year. Rheumatology also participates in the Supporting Structures Course of the IMS curriculum at the Brown Medical

School. Dr. Schwartz continues to be the course Director for the Supporting Structures Course in the second year. Moreover, both Dr. Lally and Dr. Schwartz provide office-based teaching for residents in addition to presenting monthly noontime House Staff Conferences on a variety of rheumatic diseases.

With the full support of Dr. Edward Wing, Chairman of Medicine and Physician in Chief, the Division of Rheumatology is committed to foster collaborations with the other Divisions within the Department of Medicine. There is also considerable interest in developing collaborations with other Departments especially the Department of Orthopedic Surgery and the Department of Dermatology. Given the resources available at Rhode Island Hospital and throughout the Brown system, the Division of Rheumatology will grow and achieve the high stature of all of the other Divisions within the Department of Medicine.

For more information please contact Dr. Edward Lally at (401) 444-2248.

Faculty Promotions and Appointments Full Time and (Research) Faculty Appointments

Rhode Island Hospital

Cardiology

—Correction

Ulrike Mende, MD

Associate Professor, Research Scholar Track

Bum-Rak Choi, Ph.D.

Assistant Professor (Res.)

Pulmonary & Critical Care

Sean Townsend, MD, Assistant Professor

Graduate Medical Education

Brown Medical School Internal Medicine Residency Program

Rhode Island Hospital – The Miriam Hospital – VA Medical Center

Practicing What She Teaches

Dr. Kelly A. McGarry provides exceptional care to her patients and is training the next generation of physicians to do the same.

If it is her objective to single-handedly improve the health of women in this country, Dr. Kelly McGarry is well on her way.

Brown Medical School is replete with doctors who have distinguished themselves, their institution and their profession. In such select company, McGarry is in a class by herself, according to her boss, Dr. Michelle G. Cyr, associate dean of medicine.

“She was clearly the best chief medical resident with whom I have worked during my 20 years at Brown Medical School,” Cyr said, recounting the medical school’s recruitment of McGarry to its general internal medicine faculty in 1996.

She has been an assistant professor of medicine at Brown since 2000. Academically, McGarry focuses her research on osteoporosis, substance abuse and lesbian health care.

She has served as co-investigator on four osteoporosis grants and co-principal investigator for a grant from the Lesbian Health Fund. She publishes in these areas, contributes chapters to medical textbooks, and frequently speaks locally and nationally on women’s health. She and a colleague are editing a textbook on women’s health, to be released next year.

Currently, McGarry is establishing a women’s health concentration for future doctors in the Brown residency program. Last year, she became education director for the National Center of Excellence in Women’s Health at Brown and Women & Infants Hospital. In this capacity, she evaluates and enhances the medical school’s women’s health curriculum.

In 1998, asked to oversee the education of doctors doing their residencies at Brown, she developed and implemented an extensive primary care internal medicine curriculum, emphasizing the care of underserved populations, women’s health and cultural competence. Meeting regularly with the 30 residents in her charge, she helps shape doctors just entering the profession, providing feedback and career advice. She has been a role model to hundreds of medical students and residents during her tenure.

McGarry is dedicated to her work teaching medical interns and residents, and it shows. Her students consistently identify her as one of the best internal medicine attendings at Brown, recognizing her humanism and outstanding teaching. In 2000, McGarry received the prestigious Medical Educator Award from the Society of General Internal Medicine, New England region.



Photo Courtesy of Agneta Productions

In addition to her academic research and writing, and her work with interns and residents, McGarry maintains a very busy women’s health practice. She also volunteers regularly at the Rhode Island Free Clinic, working with students and residents to provide free health care to Rhode Islanders.

Among an impressive list of awards, McGarry was chosen “Best Doctor in America” in 2003 and again in 2005, and “Top Doc for Women” by Rhode Island Monthly magazine in 2003.

A native Rhode Islander, McGarry graduated Brown University in 1992, earned her medical doctorate at Yale University, and returned to Brown for her residency.

Not yet 40, McGarry has focused her considerable talents, knowledge and skill to make a difference in the health—and lives—of women.

Or as her boss, Dr. Cyr, says, “Kelly has dedicated herself to providing exceptional care to her patients and to training the next generation of physicians to do the same.”

Rhode Island women are lucky to have her.

Reprinted Courtesy of “*She Shines Staff*.”

She Shines is a magazine celebrating the aspirations and accomplishments of women and is published by the YWCA Northern Rhode Island

Office of the Chairman of Medicine
Rhode Island Hospital
593 Eddy Street
Providence, RI 02903

Department of Medicine Grand Rounds - Tuesday Mornings at 8:00 AM

George Auditorium, Rhode Island Hospital

Lecture Hall, The Miriam Hospital, Room 653, VA Medical Center • Library Video Room, Newport Hospital (teleconferenced from RIH)

November 7, 2006:

Emergency Medicine Update
"2006 Update in the Management of TIA
and Acute Ischemic Stroke"

Peter D. Panagos, M.D., Associate Director,
RIH Comprehensive Stroke Center,
Attending Physician, Rhode Island Hospital
and The Miriam Hospital, Assistant
Professor, Department of Emergency
Medicine, Brown Medical School

November 14, 2006:

"Clinical Utility of Physical Performance
Measures in Older Adults: An Update for
Internists"

Matteo Cesari, M.D., Ph.D., Clinical Staff
Fellow, Geriatric Acute Care Unit,
Department of Gerontology, Geriatrics and
Physiatry, Catholic University of Sacred
Heart, Rome, Italy

November 21, 2006:

Morbidity & Mortality Conference

November 28, 2006:

Nephrology Update

December 5, 2006:

Morbidity & Mortality Conference

December 12, 2006:

"Developments in antifungal therapy:
More choices, new challenges"

Eleftherios E. Mylonakis, M.D., Ph.D.,
Clinical Assistant in Medicine, Assistant
in Medicine, Division of Infectious Diseases,
Massachusetts General Hospital, Assistant
Professor of Medicine, Harvard Medical School

December 19, 2006:

Gastroenterology Update

December 26, 2006:

CANCELED - HAPPY HOLIDAY

January 2, 2007:

CANCELED

January 9, 2007:

The Galkin Lecture

Catherine Wilfert, M.D., Professor Emerita
of Pediatrics & Microbiology, Duke
University Med. Ctr; Scientific Director,
Pediatric AIDS Foundation, Duke Children's
Hospital and Health Center

January 16, 2007:

Cardiology Imaging Update

James Arrighi, M.D., Associate Professor,
Brown Medical School

January 23, 2007:

Morbidity & Mortality Conference

January 30, 2007:

"Amyloidosis"

Martha Skinner, M.D., Professor of
Medicine, Director of the Amyloid Program,
Boston University School of Medicine